ORIGINAL ARTICLE

Rev Bras Cir Cardiovasc 2011; 26.1: 86-92

Long-term results of septal myectomy in the treatment of obstructive hypertrophic cardiomyopathy

Resultados a longo prazo da miectomia septal no tratamento da cardiomiopatia hipertrófica obstrutiva

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RBCCV 44205-1250

Abstract

Objective: **To evaluate clinical and late echocardiography of septal myectomy surgery in patients with hypertrophic obstructive cardiomyopathy (HOCM). Methods: We examined retrospectively 34 consecutive adult patients (age 55.7±15.2 years) with HOCM operated on in our institution from 1988 to 2008. Only four patients (11.8%) had family history of OHCM. Nine patients (26.5%) were in New York Heart Association (NYHA) functional class IV. Thirty patients (88.2%) had only HOCM, and four (11.8%) had HOCM associated with coronary insufficiency. The surgical technique used in all patients was septal myectomy performed through an aortotomy.**

Results: **In 26 patients (76.5%) the mitral insufficiency due to anterior systolic motion decreased after the myectomy. Eight patients (23.5%) had mitral valve procedures. There was one in-hospital death (2.9%). Two patients (5.9%) required permanent pacemaker for complete heart block after the myectomy. The mean peak preoperative left ventricular outflow tract (LVOT) obstruction gradient was 84.9±29.0 mmHg, and decreased to 27.8±12.9 mmHg in the early postoperative, and it was 19.2±11.2 mmHg in the late postoperative period (49.0±33.0 months). The NYHA functional class improved from 3.1±0.8 to 1.4±0.5 in the postoperative period. Survival free from death was 87.9% and survival free from cardiovascular events was 77.7% with a mean follow-up of 9.6±8.4 years.**

Conclusions: **Surgical septal myectomy can be performed safely, with excellent survival, improvement from symptoms and relief for LVOT obstruction in patients with HOCM. The early benefits were remained at long term.**

Descriptors: **Thoracic Surgery. Treatment Outcome. Cardiomyopathy, Hypertrophic. Long-term Effect. Cardiovascular Surgical Procedures.**

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Article received on July 26th, 2010
Article accepted on December 6th, 2010

Resumo

Objetivo: **Avaliação clínica e ecocardiográfica tardia da miectomia septal cirúrgica de pacientes com cardiomiopatia hipertrófica obstrutiva (CMHO).**

Métodos: **Foram analisados, retrospectivamente, 34 pacientes adultos (média de 55,7±15,2 anos) portadores de CMHO operados consecutivamente na instituição entre 1988 e 2008. Apenas quatro (11,8%) pacientes tinham conhecimento de história familiar para CMHO. Nove (26,5%) pacientes apresentavam insuficiência cardíaca (NYHA) classe funcional IV. Trinta (88,2%) pacientes apresentavam CMHO isolada e, em quatro (11,8%), a CMHO estava associada à insuficiência coronária. A técnica cirúrgica utilizada em todos os casos foi a miectomia septal transaórtica.**

Resultados: **Em 26 (76,5%) pacientes, a insuficiência mitral decorrente do movimento anterior sistólico regrediu após a miectomia. Em oito (23,5%) pacientes, houve necessidade de abordagem da valva mitral. Houve um (2,9%) óbito hospitalar. Dois (5,9%) pacientes necessitaram de marcapasso definitivo no pós-operatório. Em média, o gradiente de pico pré-operatório na via de saída do ventrículo esquerdo, que era de 84,9±29,0 mmHg, diminuiu para 27,8±12,9 mmHg no pós-operatório inicial e caiu para 19,2±11,2 mmHg no pós-operatório tardio (49,0±33,0 meses). A classe funcional (NYHA) que, em média, era de 3,1±0,8 passou para 1,4±0,5 no pós-operatório. Com seguimento médio de 9,6±8,4 anos, a sobrevida foi de 87,9% e a sobrevida livre de eventos cardiovasculares foi de 77,7%.**

Conclusão: **A miectomia septal cirúrgica pode ser realizada de modo seguro, com excelente sobrevida, melhora dos sintomas e alívio da obstrução na via de saída do ventrículo esquerdo em pacientes com CMHO. Os benefícios iniciais se mantiveram a longo prazo.**

Descritores: **Cardiomiopatia Hipertrófica. Procedimentos Cirúrgicos Cardiovasculares. Resultado de Tratamento. Efeitos a Longo Prazo.**

INTRODUCTION

Hypertrophic obstructive cardiomyopathy (HOCM) is a genetic disorder characterized by a marked myocardial fibers disarray [1,2]. Its symptoms can range from dyspnea to arrhythmia and heart failure, embolic events and sudden death [3,4]. The dynamic obstruction of the left ventricle outflow tract associated with the anterior systolic motion of mitral valve are responsible for the deleterious effects of this disease [5,6]. The prognosis of patients is related to the presence of symptoms and especially to the degree of septal hypertrophy and the pressure gradient in the left ventricular outflow tract [70-10].

Over the years, septal myectomy surgery has been proven to be a safe and effective procedure in reducing the left ventricular outflow obstruction with relief of the symptoms and improved quality of life in otherwise symptomatic patients and not responding to optimal medical treatment [3,4,10-13]. In most cases, the mitral insufficiency or changes in the subvalvular apparatus can be corrected without being necessary to replace the mitral valve [14,15]. Although it is not a complex procedure, the learning curve of surgical septal myectomy is long and requires a considerable hands-on experience as well as academic training to perform a good reduction of left ventricular outflow obstruction tract without causing complications, such as a ventricular septal defect, aortic valve injury, and complete atrioventricular block; besides performing mitral valve repair when necessary.

Percutaneous techniques with alcohol ablation to induce localized septal infarction have Been used since 1995 [16,17]. These procedures, which seek to relieve the left ventricular obstruction and reduce systolic anterior motion of mitral valve have become widely accepted and have presented rapid growth [18].

Currently, surgical septal myectomy has been challenged by percutaneous techniques, which are less invasive and therefore, more attractive than the surgery itself. Several studies have compared both techniques in an attempt to find a greater benefit out of one of the two procedures [19,20]. In this contest, we will show the current experience with surgical septal myectomy in patients with HOCM.

METHODS

Thirty-four consecutive adult patients with HOCM operated on at the institution during 20 years (September 1988 to December 2008) have been retrospectively analyzed. The patients mean age ranged from 19 to 78 years (mean plus or minus Standard Deviation (SD) of 55.7 ± 152). Only four patients (11.8%) were aware of the family history of HOCM and 21 patients (61.8%) had difficulty controlling systemic hypertension. Sixteen patients (47.1%) had NYHA functional class III for heart failure, nine patients (26.5%) were in functional class IV, and five (14.7%) had histories of syncope in an advanced stage of the disease. One patient had a prior history of central neurological changes, requiring tracheotomy caused by a stroke.

In all cases, the diagnosis was confirmed by transthoracic Doppler echocardiography, relying on the degree of septal hypertrophy and the pressure gradient at rest in the left ventricular outflow tract. Thirty patients (88.2%) had HOCM with small or moderate mitral regurgitation due to systolic anterior motion of mitral valve, and in four patients (11.8%) the mitral regurgitation was important. The maximum gradient in the left ventricular

outflow ranged from 30 mmHg to 140 mmHg (84.9 ± 29.0 mm Hg) and septal thickness ranged from 13 mm to 30 mm (21.6 ± 4, 1 mm). Coronary artery disease was associated to four (11.8%) patients (Table 1).

Table 1. Preoperative chacracteristics (n=34)

	N (%)
Gender (F / M)	19/15 (55.9%/44.1%)
Age (years)	19-78 (55.7 anos±15.2)
NYHA CHF functional class III/IV	25 (73.5%)
SAH	21 (61.8%)
Diabetes Mellitus	4 (11.8%)
Syncope	5 (14.7%)
Family History for HOCM	4 (11.8%)
Severe Mitral Insufficiency (regurgitation)	4 (11.8%)
Heart Failure	4 (11.8%)
Prior Stroke (CVA)	1 (2.9%)
Chronic Atrial Fibrillation	1 (2.9%)
Prior Alcoholic Embolization	1 (2.9%)
LV outflow maximum gradiente(mmHg)	30–140 (84.9 ± 29.0)
Thickness of myocardial septum (mm)	13–30 (21.6 ± 4.1)

F: Female. M: Male. CHF: Congestive Heart Failure. NYHA: New York Heart Association.
SAH: Systemic Arterial Hypertension. HOCM: Hypertrophic Obstructive Cardiomyopathy. AVC: Cerebral Vascular Accident (Stroke). LV: Left Ventricle

The time between diagnosis and surgical treatment of the disease ranged from 6 months to 13 years (5.9 years ± 3.8 years). The technique used to correct the left ventricular outflow obstruction tract showed small variations relative to the needs of each case; however, the main basic points were always the same, as classically described by Morrow [21]: median sternotomy, cardiopulmonary bypass support, mild systemic hypothermia, hypothermic cardioplegia, transverse aortotomy, and transaortic (or trans-septal) septal approach with implementation of septal myectomy. In general, myectomy was performed with the removal of a rectangular segment of the basal septum. It was performed making two parallel longitudinal incisions beginning just below the membranous septum and extending as far as the obstruction of the septal portion, where they were joined together. In some cases the incisions extended down as far as to the base of the papillary muscles.

This study was approved by the Scientific and Medical Ethics Committee of the Heart Institute of the University of São Paulo School of Medicine Clinics Hospital (InCor HCFMUSP). Data were initially collected from the database of the Heart Institute and from the evaluation of medical records. Clinical and echocardiographic follow-up was carried out using medical records, phone interview questionnaires, and when was the case, clinical consultation.

The statistical analysis initially consisted of the demographic data of the 34 patients, such as the study population characteristics, degree of left ventricular outflow obstruction tract, surgical procedure, intra- and postoperative complications, immediate postoperative and late echocardiogram, and the occurrence of cardiac events. Classificatory variables were descriptively presented in contingency tables showing absolute (n) and relative (%) frequencies. Quantitative variables were descriptively presented in tables with mean plus or minus Standard Deviation (SD). The variables' septum and the left ventricular outflow tract gradient were parametrically evaluated using the analysis of variance for repeated measures. The probability of survival and events over time were estimated using the Kaplan-Meier method. P values <0.05 were considered significant. The SAS system (Statistical Analysis System) was used for all tests. The tests were performed by the Department of Statistics.

Table 2. Associated Surgical Proedures (n=34)

	N (%)
Isolated Septal Myectomy with Mitral insufficiency regression	26 (76.5%)
Mitral Valva approach	8 (23.5%)
Myocardial Revascularization (Cardiopulmonary Bypass)	4 (11.8%)
Aortic Valve Repair	1 (2.9%)
Correction of Atrial Fibrillation through Ablation	1 (2.9%)

RESULTS

All 34 patients underwent transaortic septal myectomy surgery. In 26 patients (76.5%), the procedure was isolated with spontaneous regression of mitral regurgitation due to systolic anterior motion. Eight patients (23.5%) needed associated procedures (Table 2). There was one in-hospital death (2.9%) relative to a 73-year-old patient, who underwent septal myectomy associated with mitral valve repair. He presented myocardial dysfunction after a cardiopulmonary bypass. One patient had a minimal interventricular communication (IVC) postoperatively, and he was clinically followed-up. One patient required a permanent pacemaker because of a complete atrioventricular block (CAVB), and another one needed an implantable cardioverter-defibrillator (ICD) due to associated episodes of ventricular tachycardia (VT). There were two (5.9%) strokes (cerebral vascular accident (CVAs), one patient recovered completely and one remained with sequelae (Table 3). During the 1-year follow-up, we had two more deaths (6.1%): one resulting from complications of a stroke, which occurred postoperatively, and one death with due to complete atrioventricular block and progressive heart failure.

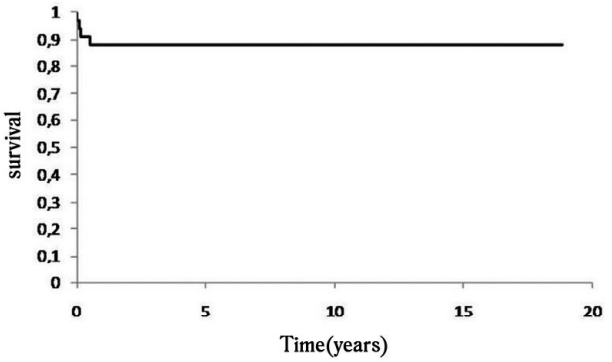

Fig. 1 - Probability of survival up to 20 years of follow up (mean 9.6 ± 8.4 years). Kaplan Meier

In late clinical follow-up, we had another death from noncardiac causes (Figure 1). Thirty patients are still being followed-up, including one patient, that is now 78-year-old, who was operated on, in 2002, showing at the present moment, good postoperative clinical outcome, and a 74-year-old patient operated on in 1994, that developed coronary heart disease in 2005. He underwent coronary angioplasty of left anterior descending and diagonal of the left coronary artery. A 55-year-old patient operated on in 2001, developed severe mitral regurgitation and atrial fibrillation (AF). He was re-operated after 2 years because of mitral valve replacement and radiofrequency atrial ablation to correct AF. Another patient, aged 49, presented CAVB four years after the surgery and required an implantable permanent pacemaker. One patient, aged 62, is clinically well, but she is under treatment for breast cancer (Figure 2).

Table 3. Immediate Postoperative Complications (n = 5/34 - 14.7%)

	N (%)
ICVA	2 (5.9%)
Pulmonary Infection	1 (2.9%)
Definitive Pacemaker	1 (2.9%)
ICD	1 (2.9%)
In-Hopital Death*	1 (2.9%)

ICVA: Ischemic Cerebral Vascular Accident. CDI: implantable cardioverter-defibrillator.
**intra-hospital death 30 days after discharge*

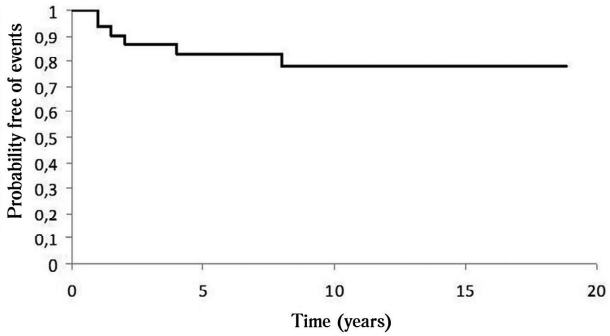

Fig. 2 - Probability free of cardiovascular events after discharge hosítalar up to 20 years of follow up (mean 9.6 ± 8.4 years). Kaplan Meier

Table 4. 1 to 20-year Postoperative Surgical Follow-up (9.6 ± 8.4 years)

	N (%)
Death	3 (9.1%)*
Reoperation	1 (3.0%)
Definitive Pacamaker	1 (3.0%)
NYAH Functional Class	1.4 ± 0.5
Survival free of cardiovascular events**	77.7%
Survival	87.9%

NYHA: New York Heart Association
** Death by noncardiac cause*
*** Arrhythmia. Cerebral vascular accident. reoperation. death*

With a mean follow-up of 9.6 ± 8.4 years (range 10-20 years), survival was 87.9% and survival free of cardiovascular events (death, arrhythmias, stroke, and reoperation) after hospital discharge was 77.7%. The NYHA functional class for heart failure that was on average 3.1 ± 0.8 (preoperatively) increased to 1.4 ± 0.5 (postoperatively) and was kept in the late follow-up period ($P < 0.001$) (Table 4). Regarding the pressure gradient in the left ventricular outflow assessed by transthoracic echocardiography, we

Table 5. Late and Immediate Postoperative Echocardiography Follow-up (49.0 ± 33.0 months).

Variable	Preoperative	I Postop.	L Postop.
Maximu pressure gradiente at left ventricular outflow tract (mmHg)	84.9±29.0	27.8 ±12.9 (P<0.001)*	19.2±11.2 (P<0.001)**
Thickness of the myocardial septum (mm)	21.6±4.1	15.8 ±3.5 (P<0.001)*	15.5±3.6 (P=0.090)**

LV = Left ventricle. I Postop. = Immediate postoperative. L postop. = Late postoperative. Mean follow-up 49.0±33.0 months
** difference in relation to preoperative period.*
*** difference in relation to immediate postoperative period*

have observed an average reduction from 84.9 ± 29.0 mmHg preoperatively to 27.8 ± 12.9 mmHg (P <0.001) in the immediate postoperative period, and to 19.2 ± 11.2 mmHg (*P* <0.001) in the late postoperative period (49.0 ± 33.0 months) (Table 5).

DISCUSSION

Recently, the advances in cardiopulmonary bypass and myocardial protection associated with the improvement of the surgical technique, and the postoperative cardiovascular surgery has caused the morbidity and mortality of septal myectomy to become progressively decreased. Currently, assistance units with extensive experience present a mortality rate between 1% and 2%, being able to reach zero in most favorable situations (9,12,13). In our experience, we had an in-hospital death (2.9%) and a survival rate of 87.9% with a mean follow-up of 9.6 years, equivalent to that observed in the international experience, with an 5-year overall survival ranging from 86% up to 96% and in 10 years between 70% and 90% [9,10,12,13]. The recent consensus of American and European Societies of Cardiology have highlighted the surgical septal myectomy as the "gold standard" to reduce the left ventricular outflow obstruction tract and to relief the symptoms in patients with hypertrophic obstructive cardiomyopathy [22].

The surgical myectomy is still questioned as to its effectiveness and morbidity, especially in relation to the atrioventricular blocks, in spite of the excellent results and the whole experience accumulated in more than four decades. In non-specialized centers, the mortality rate can be high, once the disease is uncommon and the learning curve is long. Another reason is that the percutaneous methods, such as septal alcoholization, which are less invasive, have been growing and spreading in clinical practice. Although the initial results are satisfactory, they are not free of complications and the long-term follow-up is yet not as well-known as the follow-up of the surgical outcomes [3].

The present study, despite its limited sample (34 patients), presents a mean follow up of 9.6 ± 8.4 years (range 10-20 years). Observed complications, including death from cardiac causes occurred in the perioperative period until one year postoperatively. After this period, the patients showed good survival (87.9%) and with excellent quality of life with improvement of the functional class (from 3.1 to 1.4) and myocardial remodeling represented by the further reduction of the gradient in the left ventricular outflow tract (19.2 mmHg) lately evaluated in relation to the reduction initially assessed (27.8 mmHg). Groups with extensive experience in surgical treatment of HOCM also mention excellent survival rate (95% in 10 years), suggesting that myectomy may offer the opportunity for a normal life, being equivalent to the general population and higher than the population with hypertrophic obstructive cardiomyopathy not operated on [12,13,23,24].

However, some events that occurred after myectomy have not been fully understood, suggesting that independent factors may be involved in the risk stratification of patients undergoing surgery [3, 6, 8,10]. In addition to the age (≥ 50 years), other factors have been reported and include female gender, family history of sudden death, prior history of syncope, severe septal hypertrophy, presence of ventricular tachycardia, and abnormal blood pressure response to exercise [3, 4,9,22,23]. Echocardiographic factors may also influence the long-term survival after myectomy, such as the diameter of the left atrium (≥ 46 mm) and the ratio septum/posterior wall ≥ 1.8, as well as associated procedures such as coronary artery bypass grafting [9].

While the transaortic approach to perform septal myectomy has remained the same for over 40 years, the surgical outcomes are operator-dependent. The difficulty to visualize the anatomy below the aortic valve can lead to injuries in the aortic valve itself, in the mitral valve, perforation of the left ventricular free wall, interventricular communication, complete atrioventricular block, or septal myocardial insufficient resection compromising both the initial and long-term results [22]. More recently, following the example of most experienced groups [12,13,23-26], we have gone ahead with myectomy up to the base of the papillary muscles (extended myectomy), and we have used as a routine, the intraoperative transesophageal echocardiography [15]. It is recommended that the return to cardiopulmonary bypass for expansion of septal myectomy should always be performed when the intraoperative residual gradient of the left ventricular outflow tract exceeds 20 mm Hg [22,23].

In the past 20 years only 34 patients with HOCM were operated on at the Heart Institute (InCor HCFMUSP), despite being a nation-wide reference tertiary health service and perform a high volume of cardiac surgeries. Considering that at least six different surgeons were responsible for the operations, the analysis of the outcomes turns out to be limited. Of the three patients who died of cardiac causes (one at the hospital and two in the first year after surgery) all patients had advanced age (73, 75, and 77), NYHA functional class III or IV for heart failure and gradient at the left ventricular outflow close to 100 mm Hg. However, the overall analysis of the surgical procedure (septal myectomy) brings an important contribution showing the procedure's safety and the improvement of the patient functional class, which has been maintained at long-term. In particular, the echocardiographic analysis shows that occurs a left ventricular remodeling over time decreasing the pressure gradient in the left ventricular outflow in relation to the initial postoperative condition.

Some authors attribute to this fact the higher survival among operated on patients than among non-operated HOCM patients. They also state that the survival is similar to the general population [9,10,12,23,25]. Other consistent data show that the degree of septal hypertrophy and the presence of the pressure gradient in the left ventricular outflow are related to sudden death, and this reinforces the indication for surgery [7,8]. It has also been observed that the progression of left ventricular hypertrophy is faster in children and adolescents than in adults. Besides, symptomatic children have a higher risk of death than symptomatic adults, with an annual mortality rate raging up to 6% [3].

CONCLUSION

In conclusion, symptomatic HOCM patients who are refractory to medical treatment should be considered for surgical treatment. The septal myectomy improves quality of life, allowing the ventricular remodeling. According to clinical consensuses, surgical septal myectomy remains the treatment of choice for symptomatic HOCM when considering long-term benefits.

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